

## REMARKS

### The Status of the Claims.

Claims 28, 29, and 36 to 46 are allowed.

The Examiner has noted that lines representing bonds in many formulae of the specification and figures are not dark. Replacement Sheets for Figures 1 and 2 and for specification pages 5, 13-15, 17, 20-22, 24 and 26-28 have been requested with darker lines in the chemical structures. These Replacement sheets for all of the original Figures and requested specification pages (plus page 14 which has a structure) are attached as an Appendix to this document.

Applicants submit that the Replacement Sheets merely sharpen and intensify lines on the sheets without addition of any new matter.

## **CONCLUSION**

Applicants appreciate the Notice of Allowance for the current claims. If the present document is not fully responsive to the Examiner's Comments Applicants request the Examiner contact the undersigned at (510) 769-3510 so any deficiencies can be promptly addressed.

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Respectfully submitted,



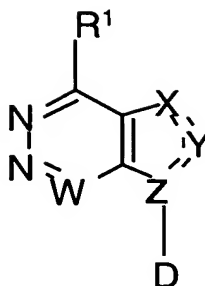
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#### Attachments:

- 1) Appendix of Replacement Sheets;
- 2) Letter to Draftsperson;
- 3) Replacements Figures 1-6 and,
- 4) A receipt indication postcard.

wherein

Formula I



5        W        is selected independently from X, Y and Z from the group consisting of N and CR<sup>2</sup>,

Z        is selected from the group consisting of N and C with the proviso that

-        if Z is N, then

10

X        independently from W and Y is selected from the group consisting of N and CR<sup>3</sup>, and

Y        independently from W and X is selected from the group consisting of N and CR<sup>4</sup>,

15

and the bond between X and Y is a double bond and the bond between Y and Z is a single bond, and

-        if Z is C, then

20

X        is NR<sup>33</sup>, and

Y        is selected from the group consisting of N and CR<sup>4</sup> and the bond between Z and Y is a double bond and the bond between X and Y is a single bond,

25

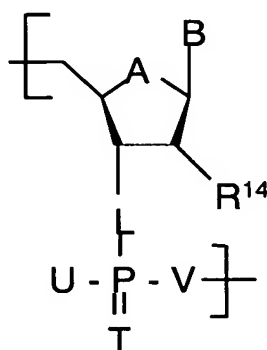
R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of -H, -halogen, -OR<sup>13</sup>, -SR<sup>19</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyl, -NO<sub>2</sub>, -NR<sup>5</sup>R<sup>6</sup>, -cyano, and -C(=O)R<sup>11</sup>,

base sequences being preferred.

The nucleic acid binding compound according to the invention will bind to nucleic acids preferably in the antiparallel mode. However, by carefully selecting the nucleobases of a  
5 nucleic acid and/or of the nucleic binding compound, the binding can also be forced to be in the parallel mode. Parallel hybridization of nucleic acids containing iso-C and iso-G are for example disclosed in EP 0 624 161.

Preferred nucleic acid binding compounds are those, wherein the backbone comprises  
10 one or more moieties of the general formula II

Formula II



wherein

- A is selected from the group consisting of O, S and N-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,  
15 L is selected from the group consisting of oxy, sulfanediyl and -NR<sup>22</sup>-,  
T is selected from the group consisting of oxo, thioxo and selenoxo,  
U is selected from the group consisting of -OH, -O-reporter group, -SH, -S  
reporter group -SeH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, (C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>6</sub>-C<sub>22</sub>)-aryl, -(C<sub>6</sub>-  
C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -NR<sup>23</sup>R<sup>24</sup>, and  
20 -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-R<sup>25</sup>, or wherein -NR<sup>23</sup>R<sup>24</sup> can together  
with N be a 5-6-membered heterocyclic ring,  
V is selected from the group consisting of oxy, sulfanediyl or -NR<sup>22</sup>-,  
R<sup>14</sup> is selected from the group consisting of -H, -OH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy,  
-(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -halogen, -azido, -O-allyl, -O-alkinyl, and -NH<sub>2</sub>,  
25 R<sup>22</sup> is independently selected from the group of -H and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

$R^{23}$  and  $R^{24}$  are independently selected from the group consisting of  $-(C_1-C_{10})$ -alkyl,  $-(C_1-C_{20})$ -aryl,  $-(C_6-C_{14})$ -aryl- $-(C_1-C_{10})$ -alkyl,  $-(C_1-C_6)$ -alkyl- $[NH(CH_2)_c]_d-NR^{26}R^{27}$  and a reporter group,

5  $R^{25}$  is selected from the group consisting of  $-H$ ,  $-OH$ ,  $-halogen$ ,  $-amino$ ,  $-(C_1-C_{18})$ -alkylamino,  $-COOH$ ,  $-CONH_2$  and  $-COO(C_1-C_4)$ -alkyl and a reporter group,

$R^{26}$  and  $R^{27}$  are independently selected from the group consisting from  $-H$ ,  $-(C_1-C_6)$ -alkyl, and  $-(C_1-C_4)$ -alkoxy- $-(C_1-C_6)$ -alkyl and a reporter group,

c is an integer from 2 to 6,  
10 d is an integer from 0 to 6, and  
B is a moiety of formula I,

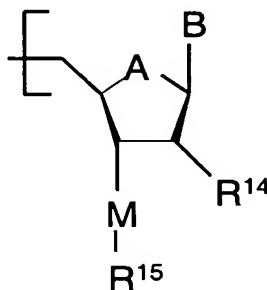
wherein any alkyl, alkenyl and alkynyl can be substituted or unsubstituted,

15 and any salts thereof.

The preferred definitions of the groups as defined under formula I apply to formula II and the following formulae, if not indicated otherwise.

20 A preferred subject of the invention is therefore a nucleic acid binding compound as outlined above, wherein the backbone comprises one or more moieties of the general formula III

Formula III

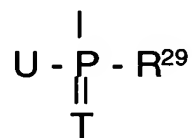


25 wherein

A is selected from the group consisting of O, S and N- $-(C_1-C_6)$ -alkyl,

- M is selected from the group consisting of oxy, sulfanediyl, -NR<sup>22</sup>-, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl-, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,
- 5 R<sup>22</sup> is selected from the group of -H, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, a protecting group and a reporter group,
- R<sup>14</sup> is selected from the group consisting of -H, -OH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyloxy, -halogen, -azido, SH, -(C<sub>1</sub>-C<sub>10</sub>)-alkylmercapto and -NH<sub>2</sub>,
- 10 R<sup>15</sup> is selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>6</sub>)-alkyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkenyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkynyl-carbonyl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, a solid phase and a group of formula IV

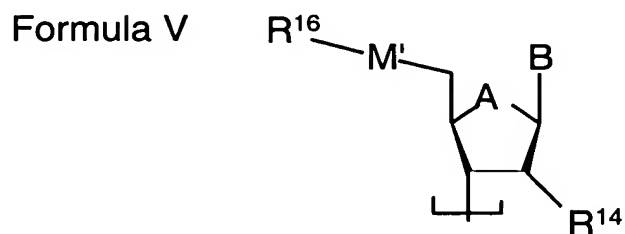
Formula IV



15 wherein

- T is selected from the group consisting of oxo, thioxo and selenoxo, and
- U is selected from the group consisting of -OH, -O-reporter group, -SH, -SeH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>6</sub>-C<sub>22</sub>)-aryl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -NR<sup>23</sup>R<sup>24</sup>, and -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-R<sup>25</sup>, or wherein
- 20 NR<sup>23</sup>R<sup>24</sup> can together with N be a 5-6-membered heterocyclic ring,
- R<sup>23</sup> and R<sup>24</sup> are independently selected from the group consisting of -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>1</sub>-C<sub>20</sub>)-aryl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>1</sub>-C<sub>6</sub>)-alkyl-[NH(CH<sub>2</sub>)<sub>c</sub>]<sub>d</sub>-NR<sup>26</sup>R<sup>27</sup>,
- 25 R<sup>25</sup> is selected from the group consisting of -H, -OH, -halogen, -amino, -(C<sub>1</sub>-C<sub>18</sub>)-alkylamino, -COOH, -CONH<sub>2</sub> and -COO(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- R<sup>26</sup> and R<sup>27</sup> are independently selected from the group consisting from -H, -(C<sub>1</sub>-C<sub>6</sub>)-alkyl, and -(C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl
- R<sup>29</sup> is selected from the group consisting of -OR<sup>30</sup> and -SR<sup>30</sup>,

A preferred subject of the invention is a nucleic acid binding compound as outlined above comprising a backbone moiety of the formula V



5 wherein

A is selected from the group consisting of O, S and N-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,

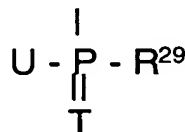
M' is selected from the group consisting of oxy, sulfanediyl, -NR<sup>22</sup>-, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,

R<sup>22</sup> is selected from the group of -H, a protecting group, a reporter group and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

R<sup>14</sup> is selected from the group consisting of -H, -OH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyloxy, -halogen, azido, -SH, -S-(C<sub>1</sub>-C<sub>6</sub>)-alkylmercapto and NH<sub>2</sub>,

R<sup>16</sup> is selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>8</sub>)-alkyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkenyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkynyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkenyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkynyl-carbonyl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, a protective group or a compound of formula IV

Formula IV



wherein

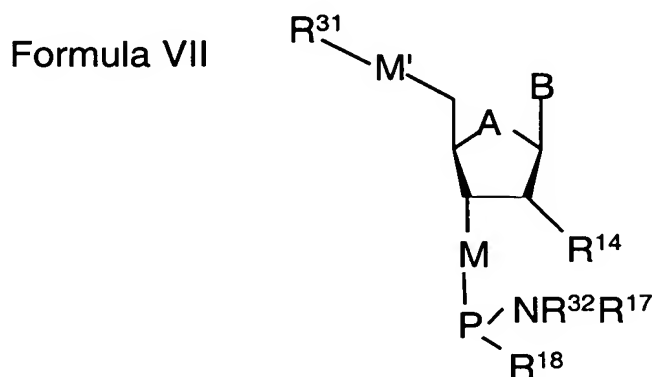
T is selected from the group consisting of oxo, thioxo and selenoxo,

U is selected from the group consisting of -OH, -SH, -SeH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>6</sub>-C<sub>22</sub>)-aryl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -NR<sup>23</sup>R<sup>24</sup>, and

The predetermined substituents are preferably selected from the group of -NH<sub>2</sub>, -SH and -OH.

A further subject of the invention is therefore a method for the chemical synthesis of  
5 a compound of any of claims 1 to 13 using activated subunits, wherein said subunit  
contains at least one group of formula I. There are several approaches known for the  
chemical synthesis, such as the phosphotriester method of Narang et al., Meth. Enzymol.  
68, 90-99 (1979); the phosphodiester method of Brown et al., Meth. Enzymol. 68, 109-  
151 (1979); the diethylphosphoramidite method of Beaucage et al., Tetrahedron Lett.  
10 22, 1859-1862 (1981); and the solid support method described in the U.S. Patent  
Specification No. 4,458,066 and in Methods in Molecular Biology, Ed. S. Agrawal, Vol.  
20, Humana Press, Totowa, NJ, 1993. The most preferred method of chemical synthesis  
uses the phosphoramidite approach. A particularly preferred method uses a activated  
subunit one or more compounds of general formula VII. This method has the advantage  
15 that it is very convenient and the reagents necessary, for example a phosphoramidite  
containing a group of formula I, is possible to be included easily.

A further subject of the invention are therefore compounds of the general formula VII



20

wherein

A is selected from the group consisting of O, S and N-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,  
M and M' are independently selected from the group consisting of oxy,  
25 sulfanediyl, -NR<sup>22</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-  
(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,  
R<sup>22</sup> is selected from the group of -H and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

$R^{14}$  is selected from the group consisting of -H,  $-OR^{31}$ ,  $-(C_1-C_{10})$ -alkoxy,  $-(C_2-C_{10})$ -alkenyloxy,  $-(C_2-C_{10})$ -alkynyloxy, -halogen, -azido  $NHR^{31}$ ,  $SR^{31}$  and  $-NH_2$ ,

$R^{31}$  is a protecting group or a reporter group,

5  $R^{32}$  and  $R^{17}$  are independently selected from the group consisting of -H,  $-(C_1-C_{10})$ -alkyl,  $-(C_2-C_{10})$ -alkenyl and  $-(C_6-C_{22})$ -aryl,

$R^{18}$  is selected from the group consisting of substituted or unsubstituted  $-(C_1-C_6)$ -alkyl, unsubstituted  $-(C_1-C_6)$ -alkoxy or  $-(C_1-C_6)$ -alkoxy substituted one or more times by a group selected from the group consisting of -halogen, p-nitroaryloxy and -cyano, and

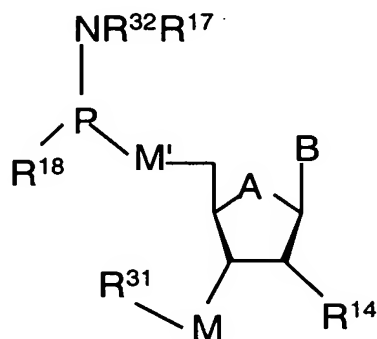
10 B is a group of formula I.

Preferred compounds of formula VII are those wherein the group of formula I is not 2-aza-hypoxanthine. In a preferred embodiment, the group of formula I in  
15 formula VII contains at least one reporter group. Most preferable, the group of formula I contains exactly one reporter group.

Most preferred in such compounds, in  $-NR^5R^6$  at least one of  $R^5$  and  $R^6$  is a protecting group.

20 Further subject of the invention are compounds of general formula IX

Formula IX



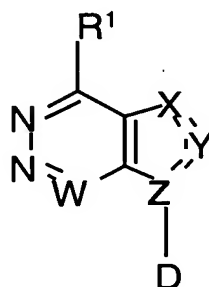
wherein

25 A is selected from the group consisting of O, S and  $N-(C_1-C_6)$ -alkyl,



- M and M' are independently selected from the group consisting of oxy,  
 sulfanediyl, -NR<sup>22</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-  
 (C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,  
 R<sup>22</sup> is selected from the group of -H and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl,  
 5 R<sup>14</sup> is selected from the group consisting of -H, -OR<sup>31</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy,  
 -(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyloxy, -halogen, -azido NHR<sup>31</sup>, SR<sup>31</sup>  
 and -NH<sub>2</sub>,  
 R<sup>31</sup> is a protecting group or a reporter group,  
 R<sup>32</sup> and R<sup>17</sup> are independently selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>10</sub>)-  
 10 alkyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyl and -(C<sub>6</sub>-C<sub>22</sub>)-aryl,  
 R<sup>18</sup> is selected from the group consisting of substituted or unsubstituted -(C<sub>1</sub>-  
 C<sub>6</sub>)-alkyl, unsubstituted -(C<sub>1</sub>-C<sub>6</sub>)-alkoxy or -(C<sub>1</sub>-C<sub>6</sub>)-alkoxy substituted one  
 or more times by a group selected from the group consisting of -halogen,  
 p-nitroaryloxy and -cyano, and  
 15 B is a group of formula I

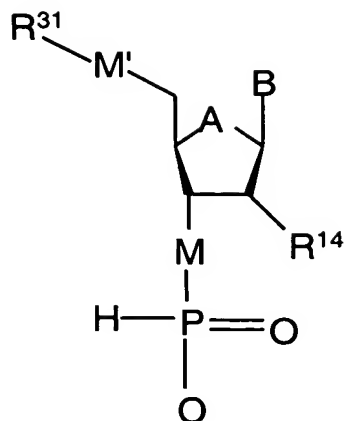
Formula I



20 wherein

- W is selected independently from X, Y and Z from the group consisting of N  
 and CR<sup>2</sup>,  
 Z is selected from the group consisting of N and C with the proviso that  
 25 - if Z is N, then

# Formula X



wherein

M and M' are independently selected from the group consisting of oxy,  
 5 sulfanediyl, -NR<sup>22</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-  
 (C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,

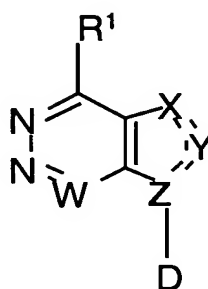
R<sup>22</sup> is selected from the group of -H and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

R<sup>14</sup> is selected from the group consisting of -H, -OR<sup>31</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy,  
 10 -(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyloxy, -halogen, -azido NHR<sup>31</sup>, SR<sup>31</sup>  
 and -NH<sub>2</sub>,

R<sup>31</sup> is a protecting group or a reporter group,

B is a group of formula I

# Formula I



wherein

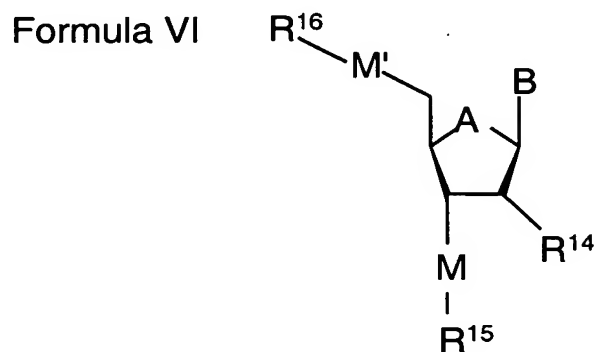
W is selected independently from X, Y and Z from the group consisting of N  
 and CR<sup>2</sup>,

In another option which is more suited for long oligomers and those based on natural backbones, the oligomers are produced enzymatically. In this case, a starting oligomer is reacted with a polymerase and a triphosphate or modified triphosphate such that a monophosphate or a modified monophosphate is attached to a terminus of the oligomer, thus elongating the oligomer. Also for this method, the man skilled in the art will know several possible formats, like the nick-translation approach, or the simple primer extension (J. Sambrook, E.F. Fritsch, T. Maniatis, Molecular Cloning - A laboratory Manual, Cold Spring Harbor Laboratory Press 1989).

For example, the incorporation of  $z^2A_d$  into a DNA sequence can be performed via conventional methods, e.g. by polymerase-catalyzed incorporation of  $z^2A_d$ -5'-triphosphate (11).

A further subject of the invention is therefore a method for the enzymatic synthesis of a nucleic acid binding compound according to the invention comprising reacting a triphosphate subunit with a primer using a nucleic acid as a template for the elongation of the primer, wherein the triphosphate subunit contains a heterocyclic group of formula I. Preferably, the triphosphate subunit has the formula VI.

A further subject of the present invention are therefore compounds of the general formula VI

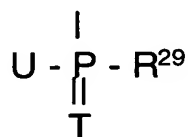


wherein

A is selected from the group consisting of O, S and N-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,

R<sup>14</sup> is selected from the group consisting of -H, -OH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, O-protecting group, S-protecting group, NH-protecting group, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -halogen, -azido, -SH, -(C<sub>1</sub>-C<sub>6</sub>)-alkylmercapto and -NH<sub>2</sub>,  
 R<sup>15</sup> and R<sup>16</sup> are independently selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>8</sub>)-alkyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkenyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkynyl, -(C<sub>2</sub>-C<sub>18</sub>)-alkyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkenyl-carbonyl, -(C<sub>3</sub>-C<sub>19</sub>)-alkynyl-carbonyl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, a protecting group or a compound of formula IV

#### Formula IV



wherein

T is selected from the group consisting of oxo, thioxo and selenoxo,  
 U is selected from the group consisting of -OH, -SH, -SeH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>6</sub>-C<sub>22</sub>)-aryl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -NR<sup>23</sup>R<sup>24</sup>, and -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-R<sup>25</sup>, or wherein NR<sup>23</sup>R<sup>24</sup> can together with N be a 5-6-membered heterocyclic ring,

R<sup>23</sup> and R<sup>24</sup> are independently selected from the group consisting of -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>1</sub>-C<sub>20</sub>)-aryl, -(C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>1</sub>-C<sub>6</sub>)-alkyl-[NH(CH<sub>2</sub>)<sub>c</sub>]<sub>d</sub>-NR<sup>26</sup>R<sup>27</sup>,

R<sup>25</sup> is selected from the group consisting of -H, -OH, -halogen, amino, -(C<sub>1</sub>-C<sub>18</sub>)-alkylamino, -COOH, -CONH<sub>2</sub> and COO(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

R<sup>26</sup> and R<sup>27</sup> are independently selected from the group consisting from -H, -(C<sub>1</sub>-C<sub>6</sub>)-alkyl, and -(C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,

R<sup>29</sup> is selected from the group consisting of -OR<sup>30</sup> and -SR<sup>30</sup>,

R<sup>30</sup> is selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, -(C<sub>2</sub>-C<sub>10</sub>)-alkenyl, -(C<sub>6</sub>-C<sub>22</sub>)-aryl, a protecting group, a diphosphate and a reporter group, and

M and M' are independently selected from the group consisting of oxy, sulfanediyl, -NR<sup>22</sup>, -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, or -O-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O-, and -S-(C<sub>1</sub>-C<sub>10</sub>)-alkyl-O- and -NR<sup>22</sup>-(C<sub>1</sub>-C<sub>6</sub>)-alkyl-O-,

R<sup>22</sup> is selected from the group of -H and -(C<sub>1</sub>-C<sub>10</sub>)-alkyl, and

B is a moiety of formula I,

wherein any alkyl, alkenyl and alkynyl can be substituted or unsubstituted, and  
wherein at least one of  $R^{15}$  and  $R^{16}$  is not a group of formula IV with the proviso  
that

$MR^{16}$ ,  $MR^{15}$  and  $R^{14}$  are not each -OH if  $R^1$  is -NH<sub>2</sub> and if either

- W and X and Y and Z is N, or
- W and X and Z is N and Y is CR<sup>4</sup>, or
- W and Y and Z is N and X is CR<sup>3</sup>.

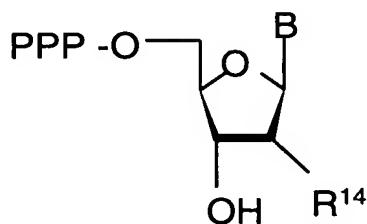
Most preferred in these compounds - $MR^{16}$  is a triphosphate group and - $MR^{15}$  is OH. The  
most preferred compound is the one in which  $R^{14}$  is -OH.

Those compounds are especially the compounds, wherein the heterocyclic moiety of the  
invention is contained not at the terminal position of the nucleic acid binding  
compound.

Preferred compounds are those, wherein M is oxy or sulfanediyl,  $R^{16}$  is a compound of  
formula IV wherein U is -OH, T is oxo or thioxo,  $R^{29}$  is -OR<sup>30</sup> and  $R^{30}$  is a disphosphate  
group and the salts thereof.

Most preferred compounds are of formula VIII

Formula VIII



wherein

PPP is a triphosphate group,

$R^{14}$  is selected from the group consisting of -H, -OH, -(C<sub>1</sub>-C<sub>10</sub>)-alkoxy,  
-(C<sub>2</sub>-C<sub>10</sub>)-alkenyloxy, -(C<sub>2</sub>-C<sub>10</sub>)-alkynyloxy halogen, -azido and NH<sub>2</sub>, and